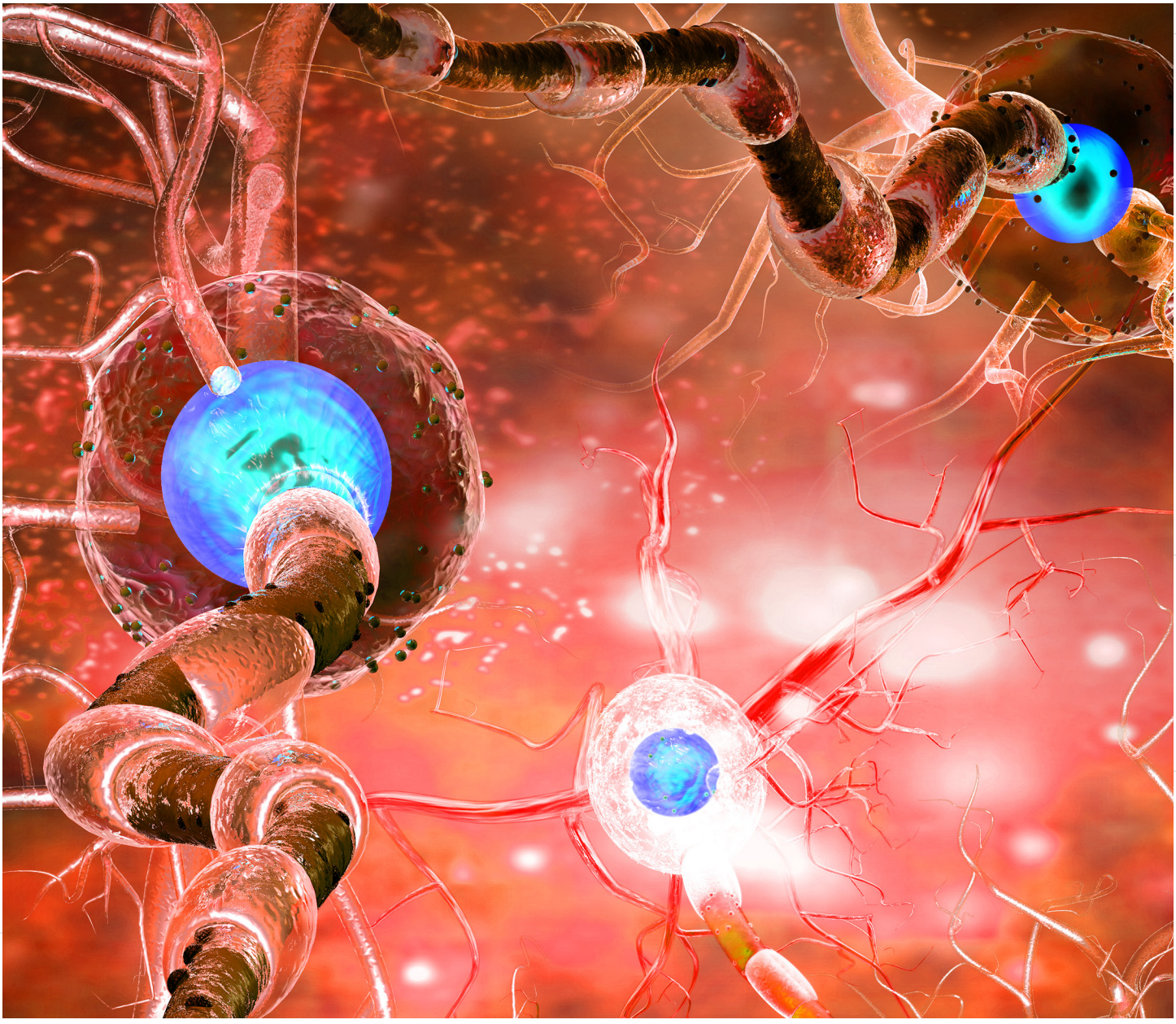
MAYO CLINIC
Mayo Medical Laboratories

AUTOIMMUNE EPILEPSY

AUTOANTIBODY EVALUATIONS TO EXPEDITE DIAGNOSIS AND TREATMENT



WHAT IS AUTOIMMUNE EPILEPSY?

Autoimmune epilepsy is caused by antibodies or cytotoxic T cells attacking cerebral cortical autoantigens. It can be diagnosed with the help of one or more informative autoantibodies specific for neural anticellular or plasma membrane antigens. Diagnosis can be further aided by a favorable response to a trial of immunotherapy.

Testing for a single autoantibody is not recommended, because limited testing may miss an autoantibody marker with high predictive value for an occult systemic cancer (i.e., paraneoplastic cases).

Patients with autoimmune epilepsy may present with new onset seizures in isolation, or with a seizure-predominant neurological disorder. Seizures in all patients reported to date have had focal or multifocal origins, rather than primary generalized. Additionally, these seizures are usually resistant to two or more standard antiepileptic medications.

CLUES HELPFUL IN IDENTIFYING PATIENTS WITH AN AUTOIMMUNE ETIOLOGY:

1. New onset epilepsy resistant to anti-epileptic medications
2. Serum autoantibody profile or CSF markers of inflammation (elevated protein or leukocytosis)
3. Greater than 50% reduction in seizure frequency with immunotherapy

WHY CONSIDER AN AUTOIMMUNE ETIOLOGY?

TO AVOID MISDIAGNOSIS OF NEURODEGENERATIVE DISORDERS

- Misdiagnosing a potentially reversible condition as a progressive neurodegenerative disorder may delay a correct diagnosis beyond the window of reversibility (6-12 months), resulting in devastating consequences for the patient and family.

BECAUSE EARLY DIAGNOSIS CAN MAKE A MEANINGFUL DIFFERENCE

- In a Mayo Clinic study of 29 patients with intractable epilepsy of suspected autoimmune etiology, 62% had significant improvement when given a trial of immunotherapy. 34% became seizure free.
- Early treatment, and maintenance immunotherapy where appropriate, gives patients the best possible outcome. Informative serological testing may also expedite the search for a limited stage cancer.

WHEN SHOULD I TEST FOR AN AUTOIMMUNE ETIOLOGY?*

CONSIDER AN AUTOIMMUNE ETIOLOGY WITH:

- New onset cryptogenic epilepsy with incomplete seizure control and of duration less than 2 years
- New onset cryptogenic epilepsy plus one or more of the following:
  - Subacute progression (maximal seizure frequency within 3 months)
  - Multiple seizure types or faciobrachial dystonic seizures
  - Anti-epileptic drug resistance
  - Psychiatric accompaniments (psychosis, hallucinations)
  - Movement disorder (myoclonus, tremor, dyskinesia)
  - Headache
  - Cognitive impairment/encephalopathy
  - Autoimmune stigmata (e.g., physical signs or personal/ family history of diabetes, thyroid disorder, vitiligo, premature graying, myasthenia gravis, rheumatoid arthritis or systemic lupus erythematosus, idiopathic adrenocortical insufficiency)
  - History of cancer
  - Smoking history (20+ pack years) or other cancer risk factors
  - Inflammatory cerebrospinal fluid
  - Neuroimages suggest inflammation (limbic or extra-temporal)

* *We strongly advise obtaining serum and CSF before starting immunotherapy*

FOR INFORMATION ABOUT DIAGNOSIS AND TREATMENT OF AUTOIMMUNE EPILEPSY, CONTACT US AT 855-516-8404

WHICH TESTS SHOULD I ORDER?

- Epilepsy Autoimmune Evaluation, CSF
  (Mayo ID: EPIEC)
  TAT: 3 days negative / 5 days positive
- Epilepsy Autoimmune Evaluation, Serum
  (Mayo ID: EPIES)
  TAT: 4 days negative / 7 days positive

WHY TEST BOTH CSF AND SERUM?

Some neural autoantibodies are detected more readily in serum (e.g., VGKC-complex IgG), while others can be detected more readily in CSF (e.g., NMDA receptor IgG). Testing both, simultaneously or sequentially, maximizes diagnostic yield.

NEURAL ANTIBODIES EVALUATED

NUCLEAR AND CYTOPLASMIC SPECIFICITIES

ANTIBODY	ONCOLOGICAL ASSOCIATION	APPROX. FREQUENCY OF CANCER
ANNA-1	Small-cell lung carcinoma, neuroblastoma, thymoma	90%
ANNA-2	Small-cell lung carcinoma, breast adenocarcinoma	90%
ANNA-3	Aerodigestive carcinoma	90%
AGNA-1 (SOX1)	Small-cell lung carcinoma	90%
PCA-2	Small-cell lung carcinoma	90%
PCA-Tr	Hodgkin lymphoma	90%
CRMP-5	Small-cell lung carcinoma, thymoma, thyroid, or renal carcinoma	90%
Amphiphysin	Small-cell lung carcinoma, breast adenocarcinoma	90%
GAD65	Occasionally (e.g., thymoma)	< 10%

PLASMA MEMBRANE SPECIFICITIES

ANTIBODY	ONCOLOGICAL ASSOCIATION	APPROX. FREQUENCY OF CANCER
VGKC-complex* (Kv1 potassium channel)	Small-cell lung carcinoma, thymoma, adenocarcinoma of breast, prostate	< 15%
NMDA receptor	Teratoma (ovarian or extra-ovarian)	50%
AMPA receptor	Thymoma, lung and breast carcinoma	70%
GABA-B receptor	Small-cell lung carcinoma, other neuroendocrine neoplasm	70%
P/Q and N-type calcium channel	Lung, breast or gynecologic carcinoma	15%
Muscle AChR	Thymoma, lung, breast, gynecologic, or prostate carcinoma	< 15%
Neuronal ganglionic AChR	Miscellaneous carcinomas, thymoma	< 15%

*VGKC radioimmunoassay sensitively detects antibodies to LGI1, CASPR2, and other VGKC-complex antigens.

Abbreviations: AGNA, anti-glial/neuronal nuclear antibody; ANNA, antineuronal nuclear antibody; PCA, Purkinje cell cytoplasmic antibody; CRMP-5, collapsin response-mediator protein-5; GAD65, glutamic acid decarboxylase-65; VGKC, voltage-gated potassium channel; NMDA, N-methyl D-aspartate; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GABA, gamma-aminobutyric acid; AChR, acetylcholine receptor.

NEUROLOGISTS STAFFING THE CLINICAL LABORATORY ARE AVAILABLE FOR CONSULTATION AND ASSISTANCE IN THE INTERPRETATION OF AUTOANTIBODY EVALUATIONS

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CLINICAL REFERENCES FOR AUTOIMMUNE EPILEPSY

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- Toledano M, Britton JW, McKeon A, et al. Utility of an immunotherapy trial in evaluating patients with presumed autoimmune epilepsy. Neurology. May 2014;82;1578-1586
- McKeon A: Paraneoplastic and other autoimmune disorders of the central nervous system. Neurohospitalist 2013 Apr;3(2):53-64

TAP INTO THE EXPERTISE OF MAYO CLINIC

The Mayo Clinic Neuroimmunology Laboratory was the first to introduce comprehensive serological evaluations to aid the diagnosis of neurological autoimmunity. The laboratory continues to discover and clinically validate novel autoantibody profiles that inform neurological decision-making and guide the search for cancer.

The clinical and research activities of the Mayo Clinic Neuroimmunology Laboratory focus on autoimmunity affecting the brain, optic nerve, retina, spinal cord, autonomic and somatic nerves and muscle. The neuroimmunology laboratory complements Mayo Clinic's Autoimmune Neurology Clinic.

FOR MORE INFORMATION ABOUT AUTOIMMUNE NEUROLOGY TESTING

MayoMedicalLaboratories.com/neurology

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